CALIFORNIA DEPARTMENT OF PESTICIDE REGULATION
MEDICAL TOXICOLOGY BRANCH
SUMMARY OF TOXICOLOGY DATA

DIMETHOATE

SB 950 # 039, Tolerance # 204
Chemical Code #: 000216
November 4, 1987
Revised 8/18/89, 11/28/89, 11/05/91, 1/8/96, 6/20/96, 9/17/96, 9/23/98

I. DATA GAP STATUS

Combined, rat:	No data gap, no adverse effect
Chronic toxicity, dog:	No data gap, no adverse effect
Oncogenicity, mouse:	No data gap, no adverse effect
Reproduction, rat:	No data gap, possible adverse effect
Teratology, rat:	No data gap, no adverse effect
Teratology, rabbit:	No data gap, no adverse effect
Gene mutation:	No data gap, no adverse effect
Chromosome effects:	No data gap, no adverse effect
DNA damage:	No data gap, possible adverse effect
Neurotoxicity:	No data gap, no adverse effect

Note: Toxicology one-liners are attached.

In the one-liners below:
** indicates an acceptable study.
Bold face indicates a possible adverse effect.
NOTE: These pages contain summaries only. Individual worksheets may identify additional effects.

File name: T980923

Revised: H. Green and M. Silva, 8/18/89; Aldous 11/28/89; Kishiyama, Aldous, and Gee, 11/05/91, P. Iyer, 1/8/96, 6/20/96 and 9/17/96, Gee, 9/23/98.

Reconciled with DPR records on file as of 9/17/96. The highest of these record numbers was 163015 (Document 204-139).

II. TOXICOLOGY ONE-LINERS AND CONCLUSIONS

COMBINED, RAT

** 204-055 (parts 1-10), 063 053805, 065991, 065992, "Report on the Study of the Toxicity of Dimethoate in Rats after 24-Month Administration in the Diet", (BASF Dept. of Toxicology, Project No. 70C0326/8241, 10/9/86). Dimethoate 96.71%, batch 611A, fed in the diet for 24 months with 50/sex/group at 0, 5, 25, and 100 ppm and with an additional 15-20/sex/group for clinicochemical and hematology measurements at 0, 1, 5, 25, and 100 ppm. General Toxicity NOEL = 25 ppm (decreased weight gain, slight anemia). Oncogenicity NOEL > 100 ppm. Plasma ChE NOEL = 25 ppm. Erythrocyte ChE NOEL = 5 ppm. Brain ChE NOEL = 1 ppm in males and 5 ppm in females. Reviewed as unacceptable, upgradeable with possible adverse effect (angiogenic tumors at several sites). (Margolis and Gee, 10/21/87). Re-reviewed with submission of record numbers 065991 (re-evaluation of microscopic slides of spleens and mesenteric lymph nodes from males) and 065992 (discussion and historical control data). Status change to ACCEPTABLE with no adverse effect. (Green & M. Silva 8/15/89).
EPA 1-liner: Core Guideline (2/2/89).

CHRONIC TOXICITY, DOG

** 204-085 096690 "Dimethoate: 12-Month Dietary Study in Beagle Dogs", (P. Burford, et al., Huntingdon Research Centre Ltd., HRC Report No. DTF 9-G/90835, 3/19/91). Dimethoate Technical, Batch 611A, purity 96.44%, was administered in the diet at concentrations of 0, 5, 20, or 125 ppm to 6 Beagle dogs/sex/group for 52 weeks. There were no mortalities nor clinical signs of toxicity. Ophthalmoscopy was negative, except for lens opacities in one high dose male and in one high dose female which were possible (equivocal) treatment effects. The most definitive effect was dose-related inhibition of brain cholinesterase (ChE) activity in both sexes at all dose levels. RBC and plasma ChE activities were both statistically significantly reduced at 125 ppm, and RBC ChE activity was often significantly reduced at 20 ppm. In livers, there were increased numbers of sinusoidal cells containing pigment (presumed to be Kupffer cells containing hemosiderin) in both sexes at all dose levels, but without dose-response relationship. There were no strong indications of hemolysis as a major cause of such pigments. The liver pigmentation and brain ChE findings were considered sufficiently noteworthy that CDFA was advised of these findings in advance of completion of the final report (see 078:090993). Neither of these findings warrants flagging this study as a "possible adverse effect", for reasons given in the discussion section of this review. **Acceptable**. (Kishiyama and Aldous, 11/05/91).

204-078 090993 Preliminary report of brain ChE effects and liver findings in study 085:096690, above (no separate review).

ONCOGENICITY, RAT

(see combined, record # 053805)

204-031 910667 "Bioassay of Dimethoate for Possible Carcinogenicity: Rat." (NCI, report # NCI-CG-TR-4, 1/77), technical grade, no purity stated. Fed at 155 or 310 ppm to 50

males/group and 192 or 384 ppm to 50 females/group for 80 weeks followed by 33 weeks observation. UNACCEPTABLE (summary only, no data). No adverse effect reported. (Gee 3/11/85)

EPA 1-liner: Oncogenic NOEL > 500 ppm (HDT); Levels tested =250, 500 ppm.
Core Minimum (003640).

ONCOGENICITY, MOUSE

** 204-056 (3 parts) 053806 "Report on the Study of the Toxicity of Dimethoate in Mice After 78-Week Administration in the Diet", (BASF Department of Toxicology, project no. 75C0326/8242, 9/24/86) Dimethoate, Test Substance # 82/326, Batch # 611A (supplied by Industria Prodotti Chimici, Italy), ≥ 96.71%. Doses of 0, 25, 100, and 200 ppm were administered in non-pelleted feed to 50/sex/group (main study groups) for 78 weeks and to 10/sex/group (interim sacrifice groups) for 52 weeks. Systemic NOEL = 25 ppm (liver changes). ChE NOEL < 25 ppm. Oncogenicity NOEL ≥ 200 ppm. ACCEPTABLE. No adverse effect. (Margolis 9/22/87 and Gee 10/20/87)

204-031 038200 (previously 910667), "Bioassay of Dimethoate for Possible Carcinogenicity: Mice", (NCI, report # NCI-CG-TR-4, 1/77), technical grade, no purity stated. Fed at 250 or 500 ppm to 50/sex/group for 94 weeks. UNACCEPTABLE (summary only, no data). No adverse effect reported. (Gee 3/11/85)

REPRODUCTION, RAT

NOTE: A letter from D. Allemang (of the Dimethoate Task Force) to O. Melnicoe (CDFA ---> CDPR) dated Aug. 1, 1990 states that in an ongoing rat reproduction study, there was an unexpected decrease in the mating performance in all treated F1 groups compared to respective controls. This is the basis for the indication on the first page of this Summary of a "**possible adverse effect"**. The study will be extended beyond the scope of the original protocol to further evaluate this apparent treatment effect. Aldous, 10/30/91.

**** 135, 092 147212, 112467**, "The Effect of Dimethoate on Reproductive Function of Two Generations in the Rat", (Amanda J. Brooker, et al., Huntingdon Research Centre Ltd., U.K., Report # DTF 11/91154, 10 January 1992), dimethoate with a stated purity of 96.44% was administered in the diet through 2 generations with two litters per generation at nominal concentrations of 0 (Labsure Laboratory Diet No. 2.), 1, 15, and 65ppm with 24 (2nd generation) or 28 (1st generation) Crl: CD®(SD) BR VAF/:Plus strain rats/sex/group. Cholinesterase (ChE) inhibition (compared with control values) was noted in both sexes for plasma (3% to 14% at 15 ppm and 19% to 41% at 65 ppm), erythrocyte (17% to 48% at 15 ppm and 55% to 70% at 65 ppm), and brain (8% to 32% at 15 ppm and 13% to 71% at 65 ppm). **Possible adverse reproductive effects are indicated**: reduced numbers of pregnant females were noted at 1, 15, and 65 ppm. Reproductive NOAEL = 1 ppm (Reduced number of pregnant females at 1, 15, and 65 ppm in the first mating of the F1 parents). Progeny NOAEL = 15 ppm [Reduced mean pup weights and reduced mean litter sizes (day 1) were reported at 65 ppm]. Parental NOEL = 1 ppm (erythrocyte and brain ChE inhibition in both sexes at 15 and 65 ppm). Previously reviewed as unacceptable, upgradeable upon submission of dose level justification (preliminary study used to set dosing levels), analysis of dosing material and necropsy results for animals that died or were killed prior to scheduled sacrifice (H. Green and P. Iyer, 12/18/95). Data in 135 147212

provided the necessary information and changed the status to acceptable (P. Iyer, 6/20/96).

137 148879 "The Effect of Dimethoate on Reproductive Function of Two Generations in the Rat", (Diane Allemang, of Jellinek, Schwartz and Connolly, Inc., Representative of Cheminova Agro A/S). Copy of the original COA (Certificate of Analysis) for batch #611/A from I.Pi.Ci; copy of test results of reanalysis of the test material at the termination of the study by BASF Aktiengesellschaft, copy of report summary entitled "Identification and determination of Active Ingredient Dimethoate and Impurities in One Batch of technical Dimethoate" and a copy of a report from a re-analysis of batch #611/A conducted under GLP by BASF in 1993 submitted. Supplemental data. No worksheet (P. Iyer, 9/17/96).

REPRODUCTION, MOUSE

204-043 037372, "Dimethoate: Successive Generation Studies in Mice", (American Cyanamid Central Medical Department, report # 65-65, 7/20/65), Dimethoate (Cygon), 98.3%, administered in diet at 0, 5, 15, and 50 ppm to 8 males and 16 females/group. NOEL $\geq$ 50 ppm. No toxicity was reported at any dose level. No adverse effect reported. UNACCEPTABLE, not upgradeable (no analysis of diets, justification for use of mouse vs rat and choice of dose levels not provided, no histopathology data on parents, husbandry problems). (Shimer 12/27/85 and Gee 1/17/86).

EPA 1-liner: no adverse effects on reproduction; no teratogenesis; systemic NOEL > 50 ppm (HDT); Reproduction NOEL > 50 ppm (HDT). Core Minimum (003640).

TERATOLOGY, RAT

** 204-038, -044 017133, 037374, "Effect of Dimethoate on Pregnancy of the Rat", (Huntington Research Centre, report # DTF 3/84245, 4/19/84), Dimethoate, 97.3%, administered by gavage in methyl cellulose to 25 female rats/group at 0, 3, 6, and 18 mg/kg/day on days 6-15 of gestation. All animals sacrificed at day 20. Maternal NOEL = 6 mg/kg/day (decreased weight gain, clinical observation of tremors, unsteady gait, salivation, hypersensitivity). Developmental NOEL $\geq$ 18 mg/kg/day. ACCEPTABLE. No adverse effect. (Gee 3/11/85).

EPA 1-liner: Teratogenic NOEL > 18 mg/g/day (HDT); Fetotoxic NOEL > 18 mg/kg/day (HDT); Maternal NOEL = 6 mg/g/day; Maternal LEL = 18 mg/kg/day (hypersensitivity, tremors and unsteady gait). Levels tested by gavage in CrL: COBS CD (SD) BR strain - 0, 3, 6 and 18 mg/g/day. Grade: Minimum (003913).

204-033 016838 Summary of record # 017133. (Gee 3/11/85)

204-037, 044 017132, 037373, "Preliminary Study of the Effect of Dimethoate on Pregnancy of the Rat", (Huntington Research Centre, report # DTF 1/84244, 4/19/84), Dimethoate, 97.3%, tested at 0, 3, 10, and 30 mg/kg/day y gavage in a preliminary study using 6 female Sprague-Dawley rats/group. General toxicity (reduced body weight), and slightly reduced litter and mean fetal weight at 30 mg/kg/day. No external fetal abnormalities noted. Supplemental to 017133. No adverse effect reported. (Gee 3/11/85)

204-033 016839 Summary of record # 017132, 037373.

TERATOLOGY, RABBIT

** 204-040, -044 017135, 037376, "Effect of Dimethoate on Pregnancy of the New Zealand White Rabbit (Teratology)", (Huntington Research Centre, report # DTF 4/84247, 4/19/84), Dimethoate 97.3%, administered to groups of 11-16 female New Zealand White Rabbits at 0, 10, 20, and 40 mg/kg/day on days 7-19 of gestation. Maternal NOEL = 20 mg/kg (reduced weight gain and food consumption); Developmental NOEL = 20 mg/kg (decreased fetal weights noted in high dose group). ACCEPTABLE. No adverse effect. (Oshita and Gee 3/11/85)

204-039, -044 017134, 037375, "Preliminary Investigation of Effect of Dimethoate on the New Zealand White Rabbit (Teratology)", (Huntington Research Centre, report # DTF 2/84246, 4/19/84), Dimethoate, 97.3%, tested at 0, 3, 10, and 30 mg/kg/day and at 50 and 75 mg/kg/day in a preliminary study using New Zealand White Rabbits (5-6/group or 2/group for second study). Supplemental to 017135. No adverse effect reported. (Oshita and Gee 3/11/85)

GENE MUTATION

** 204-045 037377, "Mutagenicity Testing of Dimethoate (AC 12,880) in the In Vitro CHO/HGPRT Mutation Assay" (American Cyanamid, project # 0423, 1/30/85), Dimethoate (Cygon) 97.3%, lot # 611A, tested at 0, 1000, 1500, 2000, 2700, and 3500 ug/ml + rat liver activation for 5 hours; 72-96 and 160-200 hour expression time. No adverse effect on mutation rate reported. ACCEPTABLE. (Shimer and Gee 1/17/86)

204-096 117164 "Results of an Ames Test-Mutagenicity Study" The Ames assay was performed using *Salmonella* strain TA100 with and without S-9 and concentrations of 20, 100, 500, 2500 and 5000 ug/plate. A 2.1 fold increase in revertant colonies was seen at 5000 ug/plate. A confirmatory assay at doses of 2000, 4000, 6000 and 8000 ug/plate demonstrated positive responses (2.9 and 2.1 fold increase) both with and without S-9 activation at 8000 ug/plate. For *E. coli* strain WP2, increases in revertant colonies (2 and 2.6 fold) were seen at 2500 and 5000 ug/plate. In the confirmatory assay, a dose-related positive response was seen at 4000, 6000 and 8000 ug/plate without activation (2.2, 2.4 and 3.8 fold); and a 2.6 fold increase was seen at 8000 ug/plate with activation. All other strains tested negative. Unacceptable (no data) (Iyer, P. 12/4/95).

204-033, -045 016837, 038201, 037379, "Mutagenicity Testing of Technical Cygon Systemic Insecticide (Dimethoate) in the Ames Bacterial Test (Salmonella typhimurium and Escherichia coli)", (American Cyanamid Co., Agricultural Research Division, project # 0-796, 11/16/77), Dimethoate technical tested in S. typhimurium strains TA 1535, 1537, 98, and 100 and in E. coli (WP-2 uvrA) with and without S-9 activation. S. typhimurium tested at 0, 100, 1000, and 10000 ug/plate (disc test also performed); positive controls inadequate to assure assay was working; no adverse effect reported. Positive results were reported in disc assay with E. coli and subsequently quantified in the plate assay at 10, 100, 1000, 5000, and 10000 ug/plate; increased revertants observed at 5000 and 10000 ug/plate. UNACCEPTABLE. Control for +S9 missing, no confirming experiment. **Possible adverse effect** indicated. (Gee 3/11/85)
EPA 1-liner: No positive mutagenic responses on any plates containing non- toxic doses. Grade: Acceptable (003640).

204-045 037380, "Mutagenicity Test Report: Isodimethoate (Ames: S. typhimurium and E. coli), (American Cyanamid Co., Agricultural Research Division, report # M77-486). Appendix

and general protocol for document/record # 033:016837.

Summary: the negative results in the CHO/HGPRT assay and in Salmonella are judged to carry more weight than the positive effect seen with E. coli at very high concentrations. The overall evaluation, therefore, is that the mutagenicity of dimethoate is equivocal and presents no adverse effect for gene mutation. (Gee 10/87). No change in evaluation (Iyer 12/95).

CHROMOSOME EFFECTS

204-100 119706, "Sister-chromatid exchanges in human lymphocytes induced by dimethoate, omethoate, deltamethrin, benomyl and their mixture" (P. Dolara et al., Mutation Research,1992 283: 113-118). Dimethoate and Omethoate induced a dose-related increase in the frequencies of sister-chromatid exchanges (SCEs) in human lymphocytes in vitro (P of regression lines <0.01). The pyrethroid insecticide deltamethrin and the fungicide benomyl, a tubulin venom, induced a modest increase in SCEs (p=0.053 and p=0.055 respectively). Mixtures of the four pesticides composed of 43% dimethoate, 43% omethoate , 12% deltamethrin and 1.2% benomyl at concentrations of 41.5 and 83 ug/ml induced dose-dependent increase in SCEs (p<0.01). Small differences between individuals were noted. Low concentrations of these four pesticides that did not increase SCEs when tested alone did result in SCE induction when tested as a mixture. Dimethoate demonstrated a statistically significant increase in SCEs/cell at 80 ug/ml (p<0.01). Supplemental (P. Iyer, 12/7/95).

** 204-045 037378, "Micronucleus Test (MNT)", (Pharmakon Research International, Inc., PH 309A-AC-004-84, 3/7/85), Dimethoate CL 12880, 97.3%, lot # 611A, in 0.9% saline administered in single dose ip to 4 groups (5/sex/group) at 55 mg/kg of bodyweight; groups were sacrificed at 6, 30, 48 or 72 hours after dosing. TEM positive control and saline (0.9%) control groups (5/sex/group) sacrificed at 30 hours. No adverse effect (a.i. did not induce formation of micronuclei). ACCEPTABLE**.** (Shimer and Gee 1/17/86)
EPA 1-liner: the test compound did not induce any significant increase in the number or PCE containing micronuclei from animals treated with single or multiple doses of 55 mg/kg. Grade: Unacceptable (004516).

** 204-053 051165, "Dominant Lethal Study with Dimethoate Technical in the Mouse", (Research & Consulting Co., AG, project # 039003, 7/24/85), Dimethoate technical, administered orally at 0, 5, 10, and 20 mg/kg bodyweight to 15 male mice/group for consecutive days; each male paired for 1 week with 2 different untreated nulliparous female mice for each of 8 consecutive weeks. Positive controls treated with 80 mg/kg bodyweight methyl methanesulfonate (MMS). No adverse effect. (Margolis 10/15/87 and Gee 10/19/87)
Note: study was submitted to fulfill the data requirement for DNA/other but does not qualify for that category. (Gee 10/87)

DNA DAMAGE

****204-080 091318**, "Unscheduled DNA Synthesis in Primary Hepatocytes of Male Rats In Vitro with Dimethoate Technical", (Rolf Fautz, Cytotest Cell Research GmbH & Co. KG (CCR), Germany, CCR Project 171000, 8/3/90). Dimethoate Technical, purity 96.38%, was assayed in vitro at concentrations of 7.63, 22.90, 76.33, 229.00, and 763.33 ug/ml for its potential to induce DNA damage in primary hepatocytes of male rats. Triplicate cultures were used for scoring for

unscheduled DNA synthesis and duplicates for concurrent cytotoxicity. Williams medium E and 2-acetylaminofluorene (positive) served as controls. Autoradiographic technique was used to determine the net number of grains per nucleus after 18 hours of exposure. **Possible adverse effect:** net grains/nucleus increased for the 2 high dose in experiment I and was confirmed by the highest dose in experiment II. ACCEPTABLE. (Kishiyama and Gee, 11/04/91)

204-080 091317, "Unscheduled DNA Synthesis in Primary Hepatocytes of Male Rats In Vitro with Dimethoate Technical", (Rolf Fautz, Cytotest Cell Research GmbH & Co. KG (CCR), Germany, CCR Project 160007, 7/31/90). Dimethoate Technical, purity 96.38%, was assayed in vitro, at concentrations of 23, 76, 229, 763, or 2290 ug/ml for its potential to induce DNA damage in primary hepatocytes of male rats. L-15 (vehicle) and 2-acetylaminofluorene (positive) served as controls. Hepatocytes were exposed to dimethoate for three hours in the presence of ^{3}H-thymidine in suspension in an orbital water bath. Unscheduled DNA synthesis was determined by isolating the DNA from 6 replicate cultures and counting radioactivity by liquid scintillation counting. **Possible adverse effect:** Dimethoate statistically significantly increased the incorporation of 3H-TdR into hepatocytes in a concentration related manner. Mean dpm/mg values increased for all treatments in experiment I and were confirmed at the 3 highest concentrations in experiment II. Toxicity to cells was not evident at the highest dose for either experiment, although toxicity was found in the pre-test cytotoxicity test. UNACCEPTABLE AND NOT UPGRADEABLE (method of exposure, length of treatment, method of isolation of nuclei not justified or explained, others in worksheet.) Kishiyama and Gee, 10/31/91.

** 204-089, -093, -139 098517 112898, 112900, 112902, 112903, 163015 "UDS and S-phase response in primary rat hepatocytes after in vivo exposure (in vitro labeling)." (BASF, 8/15/91, author not identified) Dimethoate, batch 611A, 96.41%, was given by oral gavage to Wistar (Chbb = THOM) male rats at 0 (0.5% carboxymethylcellulose or corn oil), 50, 100 or 200 mg/kg body weight in a single dose, 2 - 3 per group. Liver perfusion was started at 4 or 12 hours post dosing. Hepatocytes were isolated and put into culture wells with H-thymidine for 4 hours. Unscheduled DNA synthesis was determined by autoradiography. Three slides per animal were scored with about 35 cells per slide examined for a total of 100 cells. To calculate the net nuclear grains, the most heavily labeled area of a nuclear-sized area of cytoplasm was subtracted from the nuclear grain count. There was no indication of induction of UDS using this protocol. The positive control, 2-AAF, was marginally positive at 12 hours but was effective in 4 hour perfusion sample. Unacceptable, not upgradeable (method of calculating net nuclear grains). (Gee, 11/1/91). Reevaluated as upgradeable with a recounting of slides (Gee, 12/11/95). Upgraded to ACCEPTABLE status with submission of the re-evaluation of the slides for net nuclear counts in -139, 163015. (Gee, 9/22/98)

204-093 112898, 112900, 112902, 112903 are journal articles that discuss protocol for the in vivo rat hepatocyte DNA repair assay.

NEUROTOXICITY

** 204-085 096689 "Dimethoate: Acute delayed neurotoxicity in the domestic hen", (V. A. Redgrave, C. Gopinath, and A. Anderson, Huntingdon Research Centre Ltd., HRC Report No. DTF 15/901429, 3/25/91). Dimethoate, batch 611/A, purity 96.42%, administered by a single oral gavage (in water) or subcutaneous injection at a concentration of 55 mg/kg to hybrid brown laying hens. Numbers of hens allocated for 21-day observations were 8 vehicle controls, 3 TOCP positive controls, 10 dimethoate (subcutaneous treated), and 24 dimethoate (gavage).

The LD_{50} of dimethoate via gavage had been found to be 55 mg/kg/day. The same dose via subcutaneous route was uniformly lethal (death usually on day 1). Atropine (which was not protective at twice the LD_{50}) was not used in the main study, nor were hens exposed to a repeat treatment plus additional observation. TOCP hens developed signs of ataxia after 13 to 21 days, however dimethoate hens and controls did not. The dimethoate hens suffered 50% mortality (usually on day 1 after dosing), also weight losses among survivors during the first week, with an apparent b.w. rebound during subsequent weeks. Generally 3 hens/group were sacrificed at 4 hr and at 48 hr for brain cholinesterase (ChE) and for neuropathy target esterase (NTE) in brain and in spinal cord. Brain ChE was markedly inhibited at both time periods following dimethoate treatment, but only slightly following TOCP administration. On the other hand, brain NTE was markedly inhibited in TOCP hens, but only slightly in dimethoate hens. Spinal cord NTE was also markedly inhibited by TOCP, but not at all by dimethoate. Microscopic sections of cervical and thoracic spinal cord revealed small but consistent increases in axonal degeneration in TOCP hens, but brain and peripheral nerves were not affected. There were no microscopic treatment effects of dimethoate. Study is **acceptable**, with **no adverse effects.** (Kishiyama and Aldous, 11/04/91).

204-039 037381, "Dimethoate: Demyelination Studies in White Leghorn Hens", (American Cyanamid, report # 65-56, 6/25/65), Dimethoate, 98.1%, lot # W-40403-1, administered in feed for 4 weeks to 3 or 6 hens/group at 0, 65, 130 or 260 ppm. Later repeated with 6/group at 130 ppm dimethoate and 6/group at 2000 or 4000 ppm TOCP. No adverse effect reported. (no pathology of nerves reported). NOEL = 130 ppm. UNACCEPTABLE, protocol not suitable for either acute or subchronic toxicity, inadequate number of birds, birds too old (1-2+ years). (Shimer and Gee 1/17/86)
EPA 1-liner: oral LD50 for hen was 50 mg/kg. Repeated treatment at 1/2, 1/8, LD50 and lower for 4 weeks in diet (65, 130 or 260 ppm) showed no adverse nerve effect. One hen at each dose level died. Hens on 260 ppm lost 13% bodyweight. NOTE: only 6 hens per group. Grade: Minimum (003640).

204-065 070907 "The Potential of Dimethoate to Cause Organophosphate Induced Delayed Polyneuropathy (OPIDP)," was written by Marcello Lotti M.D. (Professor of Industrial Toxicology, University of Padua Medical School, Padua, Italy). He concludes there is enough information currently available in the literature, to assess potential neurotoxic effects of dimethoate. Data indicate that dimethoate and its major metabolite, omethoate, have negligible potential to cause Organophosphate Induced Delayed Polyneuropathy (OPIDP) based on studies in hens and poisoning cases in man. Omethoate inhibits acetylcholinesterase (AChE) and other esterases to a far greater degree than dimethoate (inhibits at > 5-10 mM) in in vitro studies. Omethoate has an I50 for AChE at 150 uM but for neurotoxic esterase (NTE), no inhibition was detectable up to 5 mM. The dose of dimethoate needed to induce OPIDP would exceed the lethal one by 30 times. In vivo studies (not guideline), where dimethoate was fed to hens at near lethal (unprotected) doses, showed no signs of OPIDP up to 3 months after treatment. In another study birds were fed omethoate at doses up to 240 ppm for 4 weeks. No cholinergic effects, clinical or histopathological signs of peripheral neuropathy were observed. Other studies using dimethoate or omethoate in hens showed similar results, however, none were performed according to FIFRA guidelines. Results in humans with poisoning by omethoate gave conflicting results. Although data demonstrate that there is little risk for OPIDP due to dimethoate, CDFA maintains that a guideline test for neurotoxicology should be performed. H. Green & M. Silva, 8/16/89.

204-066 071719 This volume contains an exact duplicate of 070907 as well as a letter and

other correspondence from Dr. Giorgio Chiesa, describing the intentions of the Dimethoate Task Force. M. Silva, 8/16/89.

SUPPLEMENTAL

204-100 119705, "Erythema-multiforme-like contact dermatitis from dimethoate" (D. Schena and A. Barba, Contact Dermatitis 1992: 27, 116-117). A case-report of erthytematous dermatitis in a worker accidentally exposed to dimethoate due to breakage of container. (P. Iyer, 12/18/95).